Seminário sobre Proteção Indoor e Outdoor (UVB, UVA, Luz Visível, Luz Azul e IR)

Danos dos raios UVB, UVA, HEV, IR e da luz visível nas células

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Human Skin and light: in the search for a better sun protection!
Excited states: ↑ reactivity

- AB^+ + e^- → cis→trans vision
- \(6\pi\)-com, \(4\pi\)-dis
- vit. D
- DNA
- \((AB)_2\)
- Damage
- Absorption (Abs)
- Emission (Emi)
- AB + A^*
- Photosynthesis

Photon energy (E) vs. Nuclear distance.
Do we understand the interaction of light with our skin or hair?

1. Which molecules absorb light?
2. How much light is absorbed?

Is this bad for the cell?
How bad?
Why?
UV level
Reações no DNA induzidas pela absorção de luz

~100.000 photons/s in UV
~20000 photons/s in UVB

S₀ → CI ~98%
CI → CI ~2%
CI → $T \leftrightarrow T$

~100.000 photons/s in UV
~20000 photons/s in UVB
Erythema

Histamine Receptor

Histamine Receptor

VASODILATION

ALBUMIN

FIBRINOGEN

ENDOTHELIAL CONTRACTION

EXUDATION
Synthesis of melanin
Avoids burning, photoaging.

Filtros solares “orgânicos”:
Unstable and can cause photosensitivity

Inorganic (zinc e titanium):
Photo-stable
Superior on the UVA
Low penetration and lower health hazards

Sun screens: Decrease the number of photons that penetrate:
FPS 10: From 100 photons 10 enter.
FPS 50: From 100 photons 2 enter.
How about UVA, does it affect the skin?
The role of the triplet species in photosensitization processes: absorption
The role of the triplet species photosensitization processes: Singlet state
The role of the triplet species photosensitization processes: Intersystem crossing

Quickly reacts with $O_2$
Also transfer of $e^-$, $e^-/H^+$, $H^-$

Lives longer and is reactive
Mechanisms of photosensitized oxidations

Type II

Very efficient in the presence of oxygen

RADICALS

Type I

Mechanisms of photosensitized oxidations

Favorable when PS is tightly bound to biomolecules

UVA-protection is characterized according pigmentation

Method known as PPD (Persistent Pigment Darkening) - Persistent Pigment Darkening
Radiation: UVA I & II (320-400 nm)
Energy: (8 - 25J / cm²)
Volunteers: Caucasians - skin type II V
Answer: after 2pm
Analyse: chromic
Why in certain situations, the scientific knowledge takes so long to bring benefits to the population?

UVA and human skin  


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…The potential risks of UVA exposure of human skin should be made much more widely known to the public. In this context I would like to raise an additional problem that has not had much attention so far. The introduction of sunscreens with high sun protection factors (SPF) may lead sunbathers to feel safe to stay in the sun much longer than previously. The protection against sunburn by a high SPF preparation obviously abrogates the skin’s own warning signal of redness and smarting. However, most sunscreens absorb in the UVB region only and provide no substantial protection against UVA. Even if the UVA irradiance is only about 20 times that of UVB the cumulative dose of UVA penetrating the skin during a summer holiday can be of significant biological importance. Presently, no regulations on UVA protection exist, and perhaps sunscreen manufacturers will be disinterested in UVA protection because filtering UVA would stop the skin from tanning. From the dermatological point of view an appropriate UVA filter has to be incorporated at least into sunscreens with UVB protection factors above 10. The UVA-SPF should be determined separately and should be not lower than 3. Unfortunately, none of the existing SPF regulations (FDA, DIN, Australian Standard) address this issue.

The basal layer in human squamous tumors harbors more UVA than UVB fingerprint mutations: A role for UVA in human skin carcinogenesis


UVA-photosensitization

- Bäumler et al *Biophys J* **2006**, 91, 1452;


**Flavins**

How about the Visible

And the visible light
Pigmentation induced by visible light was darker and more sustained than pigmentation induced by UVA in melano competent individuals.

Type II skin does not pigment well, neither with UVA nor with visible!!

Mahmoud...H.W. Lim et al. *J Invest Dermatol* **2010**, 130(8):2092-

J&J: NJ USA; Dermatology Detroit, Michigan USA

Does melanin cause any harm in the skin that would favor the synthesis of more melanin?
Melanin

Does melanin generate $^1\text{O}_2$?
Melanin generates singlet oxygen with irradiation in VISIBLE (532nm)

\[ ^1\text{O}_2 \]
Photolysis of melanin with visible light (400-700nm) is much faster in the presence of oxygen. Photolysis product showed the presence of a hydroperoxide at C3 of indol
Will the photosensitization of melanin affect the viability of melanocompetent cells

Melanin protects against UVB

![Graph showing cell survival under different light conditions for different cell lines.](image)
PROTOCOL OF MELANIN OVER-STIMULATION IN MELANO-COMPETENT CELLS

METHODS

B16F10 Cells

Tyr + NH₄Cl

48h

(Melanin)_n

48h

B16F10

B16F10
There is $^1\text{O}_2$ generation under visible light in cells over pigmentedated. The over pigmentation causes damages in cells.
Visible light -- singlet oxygen -- DNA damage
Does visible Light affects other cells?

Which molecule would absorb light?

UVA causes inhibition of autophagic flux!

Lamore & Wondrak *PPS* 2012, 11, 163
Very efficient photosensitizer in the visible

Brunk and Terman, Sweden
Lipofuscin x wavelength

Dark

408 nm

466 nm

522 nm

650 nm

Riboflavin

Wavelength (nm)

Absorbance (AU)
Tonolli et al Lipofuscin generated by UVA turns keratinocytes photosensitive to visible light *Journal of Investigative Dermatology* 2017
1. UVA

Lysosome

\[ \text{Autolysosome} \]

\[ \text{Lipofuscin} \]

\[ \text{O}_2 \text{ and other oxidants} \]

\[ \text{Pre-mutagenic lesions} \]

The Journal of investigative dermatology 137 (11), 2447
Visible light should be considered in skin protection strategies against photoinduced damage. It is certainly involved in photoaging and in other skin diseases.

We hope to stimulate the development of more robust sun protection agents!
Infra-red

Heat

**Inflammatory** cellular infiltration, disrupts the dermal extracellular matrix by inducing **matrix metalloproteinases**, and alters dermal structural proteins, thereby adding to premature skin aging.
Developing strategies to protect skin against visible light

Filters

Membrane protection

Antioxidant

Mertins et al Biochimica et Biophysica Acta 1848 (2015) 2180-2187

Patente de invenção: BR 10 2016 024262 2
Silica nanoparticles

\[ \text{H}_3\text{C}-\text{O-Si-O-CH}_3 + 4\text{H}_2\text{O} \xrightarrow{\text{Hidrólise}} \text{HO-Si-OH} + 4\text{HO-CH}_3 \]

\[ \text{HO-Si-OH} + \text{HO-Si-OH} \xrightarrow{\text{Condensação}} \text{HO-Si-O-Si-OH} + \text{H}_2\text{O} \]

\[ \text{HO-Si-O-Si-OH} + \left[ \text{HO-Si-OH} \right]_n \xrightarrow{\text{Polí condensação}} \text{HO-Si-O-Si-O-Si-O-Si-OH} + n\text{H}_2\text{O} \]
Nanofilm of melanin

Etapa 1: Tirosina + Precursors da Eumelanina → Revestida Tipo I

Etapa 2: Tirosina + Precursors da Eumelanina → Revestida Tipo II

Graph showing reflectance spectra for different samples:
- (a) Functionalized
- (b) Revestida Tipo I
- (c) Revestida Tipo II
- (d) Melanina Padrão

Images of nanoparticles and their reflectance spectra at various wavelengths.
Light transmission through filter and with sílica nanoparticles only

Light transmission by film made of ~2 mg melanina coated nanoparticles
Melanin-coated sílica nanoparticles have acceptable collors, and protect against the effects of visible light.
Mechanism of formation of melanin films
Can/should we avoid completely sun exposition?

The U.S. economic burden due to vitamin D insufficiency from inadequate exposure to solar UVB irradiance… was estimated at $40-56 billion, whereas the economic burden, for excess UV irradiance was estimated at $6-7 Billion (2004).

William B. Grant, Cedric F. Garland, and Michael F. Holick
UVB (290-320nm)

Cycloaddition $\times$ electrocyclic conrotatory $6\pi$

The contradiction in photobiology

Cyclobutyl-pyrimidine dimer

Photopродuct 6-4

Lehmann and Meurer *Dermatol Ther* 2010, 23, 2.
Baeke et al *Curr Opin Pharmacol* 2010, 10, 482.
Utilização de filtro solar evita a produção de vitamina D

Fig. 4. Effect of sunscreen use on circulating vitamin D status in a laboratory study after a single whole body exposure to 1MED UVB. From Matsuoka et al. [62]. Multiply by 2.599 to convert ng ml⁻¹ to nmol l⁻¹ (see baseline data in Table 3).
FAPESP, USP

CNPq, NAP-Phototech, FarmaService, CAPES,
CNRS, UJF, Cofecub, Fulbright, EU